

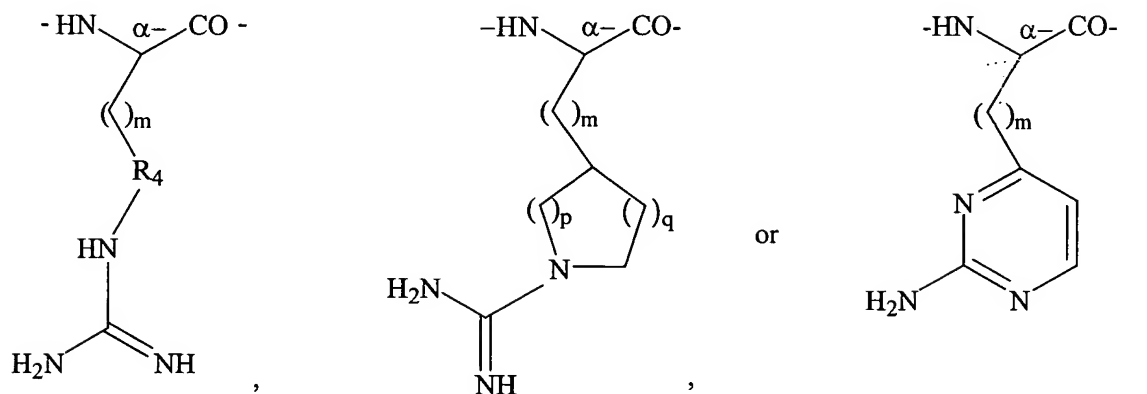
## CLAIMS

1. A peptide of structure  $\text{CM-R}_3\text{-(CA)}_n\text{-AA}_1\text{-AA}_2\text{-AA}_3\text{-AA}_4\text{-AA}_5\text{-AA}_6\text{-OH}$ , wherein said peptide has a selective affinity for neurotensin receptors and wherein
  - CM is a chelating moiety or metal binding site;
  - $\text{R}_3$  is D-lysine, D-phenylalanine, any D-amino acid, glycine-glycine-glycine, Gly-Ser-Gly, Tyr-Glu-Asn, DTyr-Glu-Asn, Phe-Glu-Asn, DPhe-Glu-Asn, piperidiny l glycine, aminomethylcyclohexylalanine, amino acid containing a cycloalkyl ring at the  $\alpha$ - or  $\beta$ -position with an amine group or an alkyl amino substituent either externally or as a part of the ring, or a spacer unit;
  - CA is a cyclic amino acid selected from the group consisting of proline, hydroxyproline, 4-oxo-proline, pipecolic acid, azetidinecarboxylic acid, and other amino acid containing a cycloalkyl ring at the  $\alpha$ - or  $\beta$ -position with an amine group or an alkyl amino substituent either externally or as a part of the ring;
  - $n = 0, 1$  or  $2$ ;
  - $\text{AA}_1$  is an amino acid which comprises a guanidino group and wherein the  $\alpha$ -carbon is either L- or D-, with the proviso that  $\text{AA}_1$  is not arginine;
  - $\text{AA}_2$  is arginine, lysine, piperidiny l glycine, or other amino acid containing a cycloalkyl ring at the  $\alpha$ - or  $\beta$ -position with an amine group or alkyl amino substituent either externally or as a part of the ring, wherein the amino acid can have the L- or D-configuration at the  $\alpha$ -carbon, or  $\text{AA}_2$  is an amino acid which comprises a guanidino group wherein the  $\alpha$ -carbon is either L- or D-;
  - $\text{AA}_3$  is a cyclic amino acid selected from proline, hydroxyproline, 4-oxo-proline, pipecolic acid, azetidinecarboxylic acid, or other amino acid containing a cycloalkyl ring at the  $\alpha$ - or  $\beta$ -position with an amine group or alkyl amino substituent either externally or as a part of the ring, wherein the amino acid can have the L- or D-configuration at the  $\alpha$ -carbon;
  - $\text{AA}_4$  is phenylalanine, tyrosine, an isomer of tyrosine, polyhydroxylated phenylalanine, or other aromatic amino acid, wherein the amino acid can have the L- or D-configuration at the  $\alpha$ -carbon;

AA<sub>5</sub> is isoleucine; and

AA<sub>6</sub> is leucine.

2. The peptide of claim 1 wherein AA<sub>1</sub> is



wherein

m = 0-6;

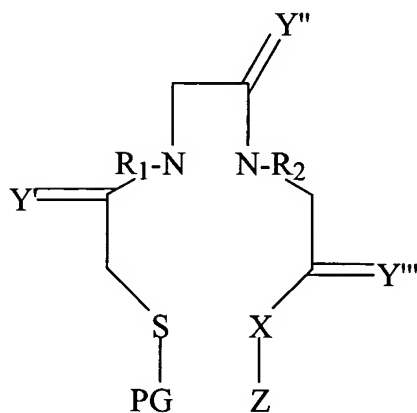
p = 1-7;

q = 1-7; and

R<sub>4</sub> is cycloalkyl C<sub>3</sub>-C<sub>10</sub>, phenyl, aralkyl, substituted phenyl or substituted aralkyl comprising an electron withdrawing or electron donating group with the proviso that said guanidino group is at a position different from said electron withdrawing or electron donating group.

3. The peptide of claim 1 wherein said peptide is labeled with a radioisotope.
4. The peptide of claim 3 wherein said label is <sup>99m</sup>Tc, <sup>203</sup>Pb, <sup>67</sup>Ga, <sup>111</sup>In, <sup>97</sup>Ru, <sup>62</sup>Cu, <sup>64</sup>Cu, <sup>186</sup>Re, <sup>188</sup>Re, <sup>90</sup>Y, <sup>121</sup>Sn, <sup>161</sup>Tb, <sup>153</sup>Sm, <sup>166</sup>Ho, <sup>105</sup>Rh, <sup>177</sup>Lu or a radioactive halogen isotope.
5. The peptide of claim 4 wherein if said label is a metal then CM is a chelating group for said metal and if said label is a halogen then said halogen is bound to an aromatic ring.

6. The peptide of claim 1 wherein CM is ethylene diamine tetraacetic acid (EDTA), diethylene triamine pentaacetic acid (DTPA), cyclohexyl 1,2-diamine tetraacetic acid (CDTA), ethyleneglycol-O,O=-bis(2-aminoethyl)-N,N,N',N'-diacetic acid (HBED), triethylene tetraamine hexaacetic acid (TTHA), 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid (DOTA), 1,4,7-triazacyclononane-N,N',N''-triacetic acid (NOTA), 1,4,8,11-tetraazacyclotetradecane-N,N',N'',N'''-tetraacetic acid (TETA) or a compound of formula



wherein

PG is a sulfur protecting group selected from the group consisting of alkanoyl, arylcarbonyl, arylalkanoyl, acetamidomethyl, tetrahydropyranyl and tetrahydrofuranyl;

Y', Y'', and Y''' are hydrogen or oxygen with the proviso that at least one of them is an O;

R<sub>1</sub> and R<sub>2</sub> are hydrogen or alkyl (C<sub>1</sub>-C<sub>3</sub>);

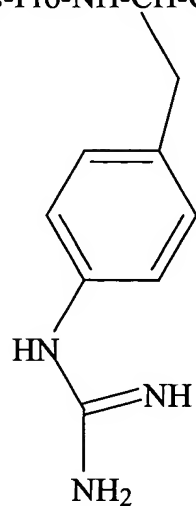
X = NH or S with the proviso that Y''' is hydrogen when X is S;

Z is PG if X is S; and

Z is hydroxyalkyl, aminoalkyl or carboxyalkyl.

7. The peptide of claim 1 wherein said peptide

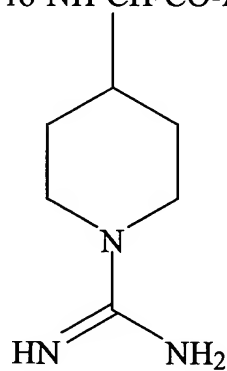
DTPA-DLys-Pro-NH-CH-CO-Arg-Pro-Tyr-Ile-Leu-OH



I

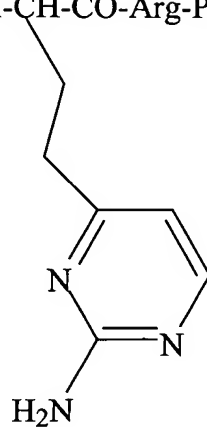
is

DTPA-DLys-Pro-NH-CH-CO-Arg-Pro-Tyr-Ile-Leu-OH



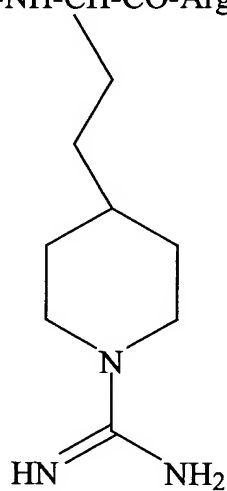
II

DTPA-DLys-Pro-NH-CH-CO-Arg-Pro-Tyr-Ile-Leu-OH



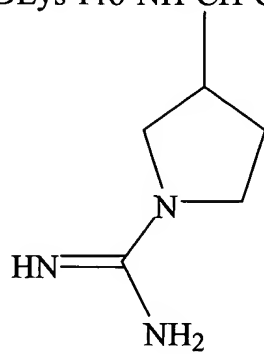
III

DTPA-DLys-Pro-NH-CH-CO-Arg-Pro-Tyr-Ile-Leu-OH

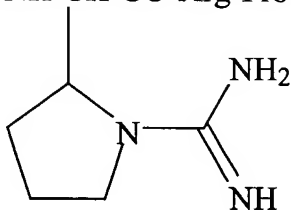


IV

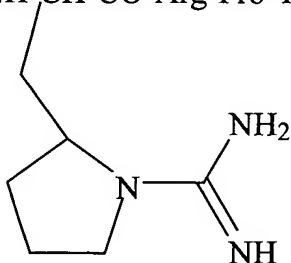
DTPA-DLys-Pro-NH-CH-CO-Arg-Pro-Tyr-Ile-Leu-OH



V

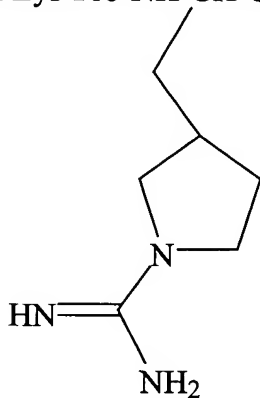


VI



VII

, or



VIII

8. A peptide of structure  $\text{CM-R}_3\text{-(CA)}_n\text{-AA}_1\text{-AA}_2\text{-AA}_3\text{-AA}_4\text{-AA}_5\text{-AA}_6\text{-OH}$ , wherein said peptide has a selective affinity for neurotensin receptors and wherein CM is a chelating moiety or metal binding site;  
 $\text{R}_3$  is D-lysine, D-phenylalanine, any D-amino acid, glycine-glycine-glycine, Gly-Ser-Gly, Tyr-Glu-Asn, DTyr-Glu-Asn, Phe-Glu-Asn, DPhe-Glu-Asn, piperidinyl glycine, aminomethylcyclohexylalanine, other amino acid containing a cycloalkyl ring at the  $\alpha$ - or

$\beta$ -position with an amine group or an alkyl amino substituent either externally or as a part of the ring, or a spacer unit;

CA is a cyclic amino acid selected from the group consisting of proline, hydroxyproline, 4-oxo-proline, pipecolic acid, azetidinecarboxylic acid, other amino acid containing a cycloalkyl ring at the  $\alpha$ - or  $\beta$ -position with an amine group or an alkyl amino substituent either externally or as a part of the ring;

$n = 0, 1$  or  $2$ ;

AA<sub>1</sub> is an amino acid which comprises a guanidino group and wherein the  $\alpha$ -carbon is either L- or D-, with the proviso that AA<sub>1</sub> is not arginine;

AA<sub>2</sub> is arginine, lysine, piperidinyglycine, or other amino acid containing a cycloalkyl ring at the  $\alpha$ - or  $\beta$ -position with an amine group or alkyl amino substituent either externally or as a part of the ring, wherein the amino acid can have the L- or D-configuration at the  $\alpha$ -carbon, or AA<sub>2</sub> is an amino acid which comprises a guanidino group wherein the  $\alpha$ -carbon is either L- or D-;

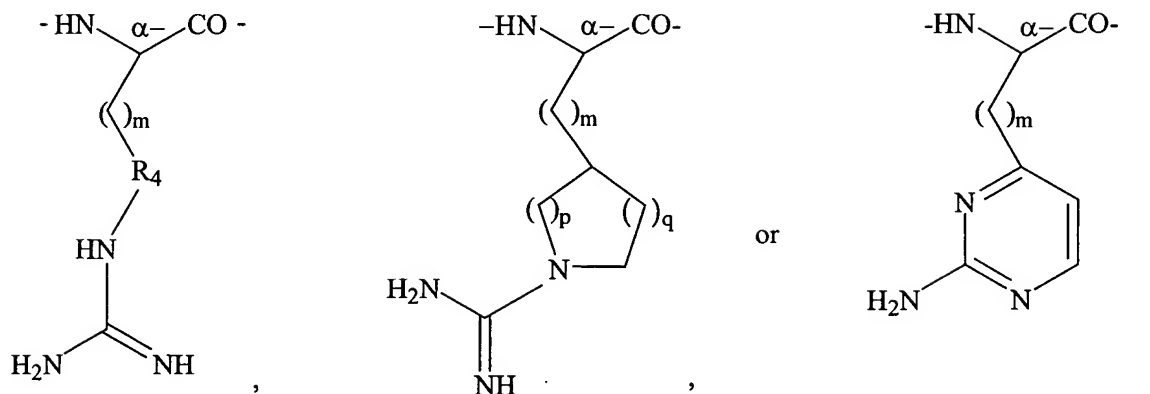
AA<sub>3</sub> is proline, hydroxyproline, 4-oxo-proline, pipecolic acid, azetidinecarboxylic acid, or other amino acid containing a cycloalkyl ring at the  $\alpha$ - or  $\beta$ -position with an amine group or alkyl amino substituent either externally or as a part of the ring, wherein the amino acid can have the L- or D-configuration at the  $\alpha$ -carbon;

AA<sub>4</sub> is phenylalanine, tyrosine, an isomer of tyrosine, polyhydroxylated phenylalanine, or other aromatic amino acid wherein said amino acid can have the L- or D-configuration at the  $\alpha$ -carbon;

AA<sub>5</sub> is t-butylglycine, 1-aminocyclohexylcarboxylic acid, cyclohexylglycine, trimethylsilylalanine, isoleucine, or other amino acid containing a branched or cyclic hydrocarbon substituent at the side chain at the  $\alpha$ - or  $\beta$ -position, wherein the amino acid can have the L- or D-configuration at the  $\alpha$ -carbon; and

AA<sub>6</sub> is cyclopropylalanine, cyclohexylalanine, t-butylalanine, leucine, or other amino acid containing a branched or cyclic hydrocarbon substituent at the side chain at the  $\alpha$ - or  $\beta$ -position, wherein the amino acid can have the L- or D-configuration at the  $\alpha$ -carbon.

9. The peptide of claim 8 wherein AA<sub>1</sub> is



$m = 0-6$ ;

$p = 1-7$ ;

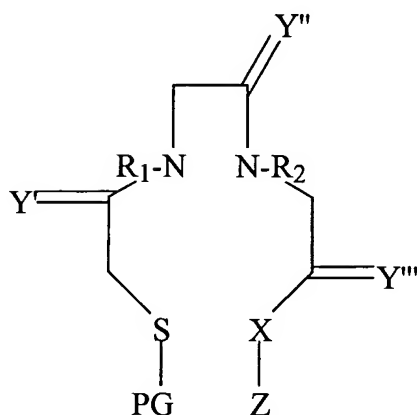
$q = 1-7$ ; and

R<sub>4</sub> is cycloalkyl C<sub>3</sub>-C<sub>10</sub>, phenyl, aralkyl, substituted phenyl or substituted aralkyl comprising an electron withdrawing or electron donating group with the proviso that said guanidino group is at a position different from said electron withdrawing or electron donating group.

10. The peptide of claim 8 wherein said peptide is labeled with a radioisotope.
11. The peptide of claim 10 wherein said label is <sup>99m</sup>Tc, <sup>203</sup>Pb, <sup>67</sup>Ga, <sup>111</sup>In, <sup>97</sup>Ru, <sup>62</sup>Cu, <sup>64</sup>Cu, <sup>186</sup>Re, <sup>188</sup>Re, <sup>90</sup>Y, <sup>121</sup>Sn, <sup>161</sup>Tb, <sup>153</sup>Sm, <sup>166</sup>Ho, <sup>105</sup>Rh, <sup>177</sup>Lu or a radioactive halogen isotope.
12. The peptide of claim 11 wherein if said label is a metal then CM is a chelating group for said metal and if said label is a halogen then said halogen is bound to an aromatic ring.
13. The peptide of claim 8 wherein CM is ethylene diamine tetraacetic acid (EDTA), diethylene triamine pentaacetic acid (DTPA), cyclohexyl 1,2-diamine tetraacetic acid (CDTA), ethyleneglycol-O,O=-bis(2-aminoethyl)-N,N,N',N'-diacetic acid (HBED), triethylene tetraamine hexaacetic acid (TTA), 1,4,7,10-tetraazacyclododecane-



N,N',N'',N'''-tetraacetic acid (DOTA), 1,4,7-triazacyclononane-N,N',N''-triacetic acid (NOTA), 1,4,8,11-tetraazacyclotetradecane-N,N',N'',N'''-tetraacetic acid (TETA) or a compound of formula



wherein

PG is a sulfur protecting group selected from the group consisting of alkanoyl, arylcarbonyl, arylalkanoyl, acetamidomethyl, tetrahydropyranyl and tetrahydrofuranyl;

Y', Y'', and Y''' are hydrogen or oxygen with the proviso that at least one of them is an O;

R<sub>1</sub> and R<sub>2</sub> are hydrogen or alkyl (C<sub>1</sub>-C<sub>3</sub>);

X = NH or S with the proviso that Y''' is hydrogen when X is S;

Z is PG if X is S, and

Z is hydroxyalkyl, aminoalkyl or carboxyalkyl.

14. The peptide of claim 8 wherein said peptide is
  - DTPA-Arg-Arg-Pro-Tyr-Ile-Leu-OH (SEQ ID NO:3),
  - DTPA-DLys-Pro-Arg-(4-Gu)Phe-Pro-Tyr-Ile-Leu-OH,
  - DTPA-DLys-Pro-(4-Gu)Phe-Arg-Pro-Tyr-Ile-Leu-OH (Compound I),
  - DTPA-DLys-Pro-(4-Gu)Phe-(4-Gu)Phe-Pro-Tyr-Ile-Leu-OH,
  - DTPA-DLys-Pro-Arg-Aba(Apy)-Pro-Tyr-Ile-Leu-OH,
  - DTPA-DLys-Pro-Aba(Apy)-Arg-Pro-Tyr-Ile-Leu-OH,
  - DTPA-DLys-Pro-Aba(Apy)-Aba(Apy)-Pro-Tyr-Ile-Leu-OH,

DTPA-DLys-Pro-(4-Gu)Phe-Arg-Pro-Tyr-tBuGly-Leu-OH (Compound IX),  
 DTPA-DLys-Pro-(4-Gu)Phe-Arg-Pro-Tyr-Leu( $\Psi$ -CH<sub>2</sub>-NH)Leu-OH,  
 DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro-Tyr-Ile-Leu-OH (Compound II),  
 DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro-Tyr-tBuGly-Leu-OH (Compound X),  
 DTPA-DLys-Pro-Gly(PipAm)-Arg-(4-oxo)Pro-Tyr-tBuGly-Leu-OH,  
 DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro-(2,6diMe)Tyr-tBuGly-Leu-OH,  
 DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro-mTyr-tBuGly-Leu-OH,  
 DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro<sup>R</sup>-OCO-Tyr-tBuGly-Leu-OH,  
 DTPA-DLys-Pro-Gly(PipAm)-PipGly-Pro-Tyr-tBuGly-Leu-OH,  
 DTPA-DLys-Pro-Gly(PipAm)-Arg-AzeCA-Tyr-tBuGly-Leu-OH,  
 DTPA-DLys-AzeCA-Gly(PipAm)-Arg-Pro-Tyr-tBuGly-Leu-OH,  
 DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro-Tyr-Ahc-Leu-OH,  
 DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro-Tyr-tBuGly-Cpa-OH,  
 DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro-Tyr-tBuGly-Cha-OH,  
 DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro-Tyr-tBuGly-tBuAla-OH,  
 DTPA-DLys-Pro-Gly(PipAm)-Arg-PipCA-Tyr-tBuGly-Leu-OH,  
 DTPA-DLys-Pro-Gly(PipAm)-Arg-DPipCA-Tyr-tBuGly-Leu-OH,  
 DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro-Tyr-Chg-Leu-OH,  
 DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro-Tyr-Ile<sup>R</sup>-OCO-Leu-OH,  
 DTPA-(Pip)Ala-Pro-Gly(PipAm)-Arg-Pro-Tyr-tBuGly-Leu-OH (SEQ ID NO:6),  
 DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro-DTyr-tBuGly-Leu-OH,  
 DTPA-DLys-Pro-Ala(PipAm)-Arg-Pro-Tyr-tBuGly-Leu-OH,  
 DTPA-DLys-Pro-homoAla(PipAm)-Arg-Pro-Tyr-tBuGly-Leu-OH,  
 DTPA-DLys-Pro-Gly(PipAm)-Arg-Pro-Tyr-tBuGly-Leu-HA,  
 DTPA-PipGly-Pro-Gly(PipAm)-Arg-Pro-Tyr-tBuGly-Leu-OH (Compound XI) (SEQ ID NO:4),  
 DTPA-*trans*-Cha(4-CH<sub>2</sub>NH<sub>2</sub>)-Pro-Gly(PipAm)-Arg-Pro-Tyr-tBuGly-Leu-OH  
 (Compound XII) (SEQ ID NO:5),

DTPA-DTyr-Glu-Asn-Lys-Pro-Gly(PipAm)-Arg-Pro-Tyr-tBuGly-Leu-OH (Compound XIII),

DTPA-DTyr-Glu-Asn-Lys-Pro-Gly(PipAm)-Arg-Pro-Tyr-tBuGly-Cha-OH (Compound XIV), or

DTPA-DTyr-Glu-Asn-Lys-Pro-Gly(PipAm)-Arg-Pro-Tyr-tBuGly-tBuAla-OH (Compound XV).

15. A method for diagnosing a patient for a tumor by administering an effective amount of a peptide of claim 1.
16. The method of claim 15 wherein said tumor is a small cell lung carcinoma, exocrine pancreatic cancer, Ewing sarcoma, meningioma, medulloblastoma, or astrocytoma.
17. A method for diagnosing a patient for a tumor by administering an effective amount of a peptide of claim 8.
18. The method of claim 17 wherein said tumor is a small cell lung carcinoma, exocrine pancreatic cancer, Ewing sarcoma, meningioma, medulloblastoma, or astrocytoma.
19. A method for treating a patient for a tumor by administering an effective amount of a peptide of claim 1.
20. The method of claim 19 wherein said tumor is a small cell lung carcinoma, exocrine pancreatic cancer, Ewing sarcoma, meningioma, medulloblastoma, or astrocytoma.
21. A method for treating a patient for a tumor by administering an effective amount of a peptide of claim 8.
22. The method of claim 21 wherein said tumor is a small cell lung carcinoma, exocrine pancreatic cancer, Ewing sarcoma, meningioma, medulloblastoma, or astrocytoma.